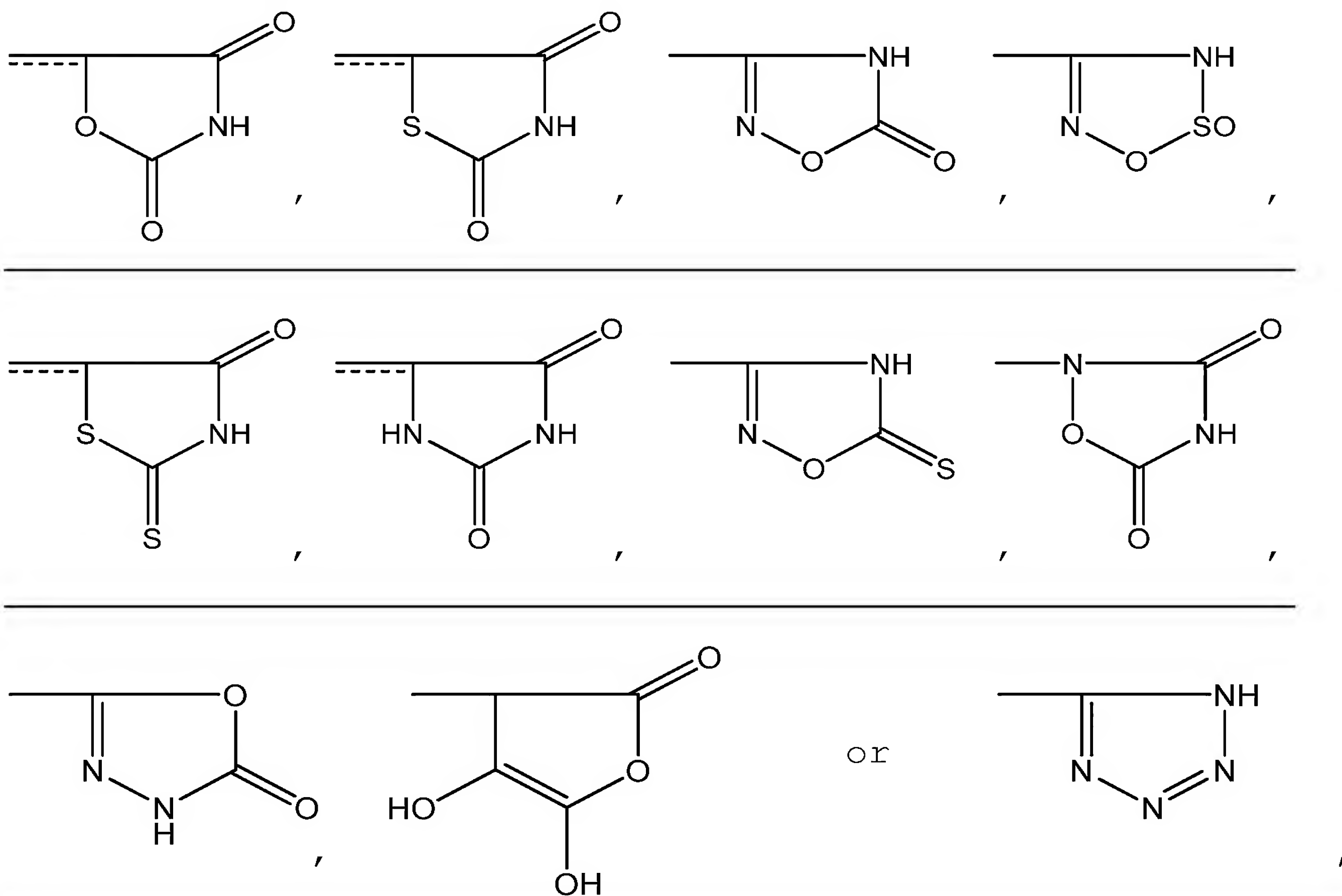
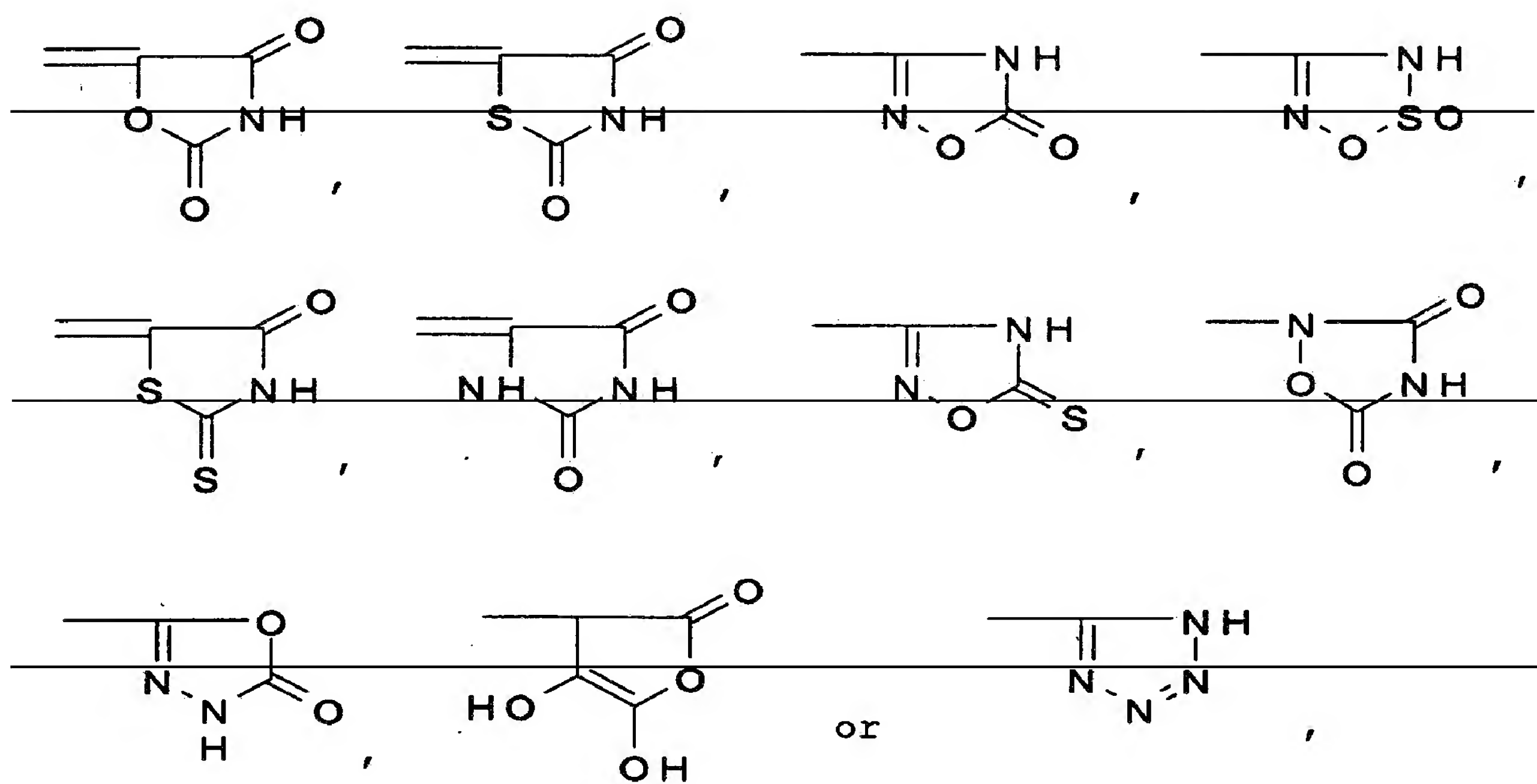


AMENDMENTS TO THE SPECIFICATION

At page 4, lines 11-13, please replace the existing paragraph with the following new paragraph:

[7] the regulator of the above-mentioned [1], wherein the group capable of releasing cation is





At page 19, lines 23-26, please replace the existing paragraph with the following new paragraph:

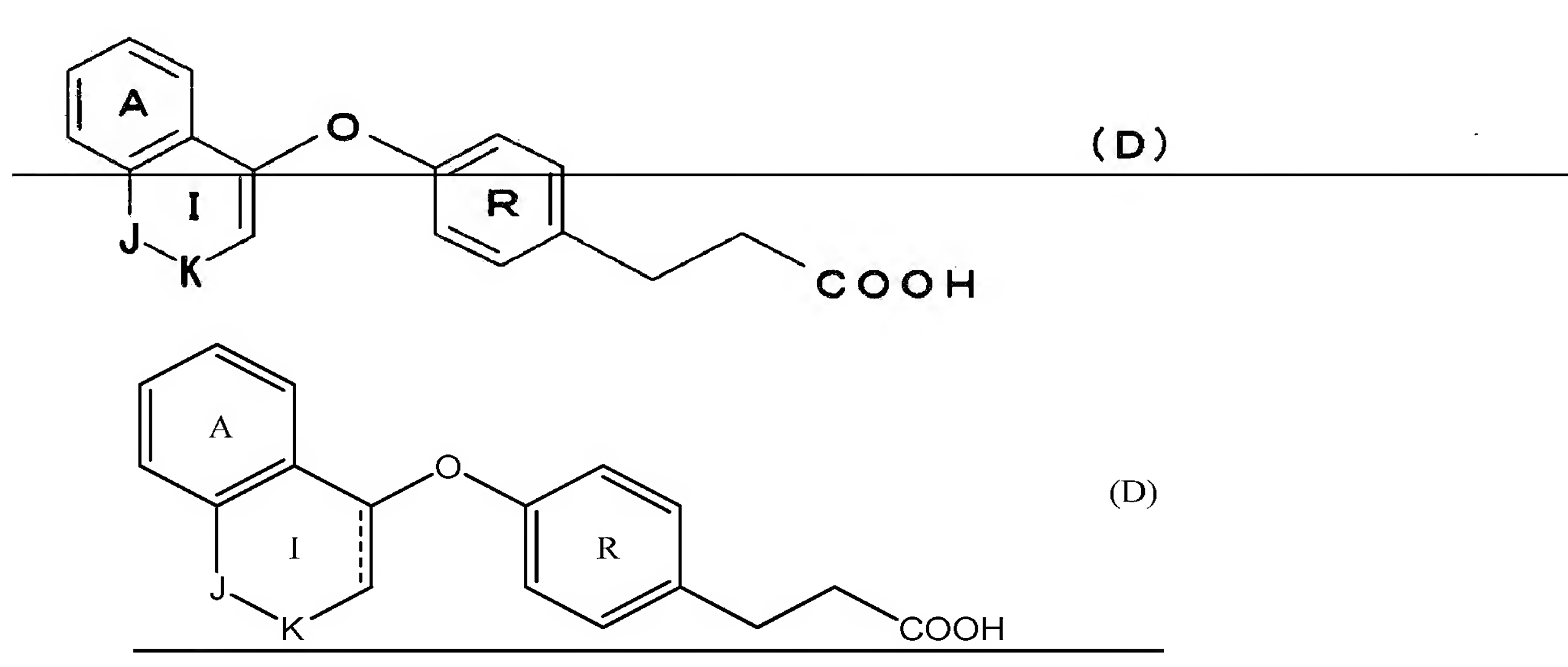
[76] the ~~compound~~ regulator of the above-mentioned [75], wherein -E²- is a bond, -O-, -CH₂-O-, -CO-, -CONH-, -N(CH₃)CH₂-, -S-CH₂- or -C=C-, preferably a bond, -O- or -CH₂-O-, ~~or a salt thereof or a prodrug thereof,~~

At page 19, line 27 – page 20, line 3, please replace the existing paragraph with the following new paragraph:

[77] the ~~compound~~ regulator of the above-mentioned [75], wherein R¹¹ is a phenyl group optionally having substituent(s) selected from the group consisting of a halogen atom, a nitro, a carboxy, an optionally halogenated C₁₋₆ alkyl, a hydroxy-C₁₋₆ alkyl, a carboxy-C₁₋₆ alkyl-carbonylamino-C₁₋₆ alkyl, an optionally halogenated C₁₋₆ ~~alkoxy~~ alkoxy, a C₆₋₁₄ aryl, a C₆₋₁₄ aryloxy and a C₇₋₁₆ aralkyloxy, ~~or a salt thereof or a prodrug thereof,~~

At page 21, line 20 - end of page 21, please replace the existing paragraph with the following new paragraph:

[83] the regulator of the above-mentioned [2], which comprises a compound represented by the formula



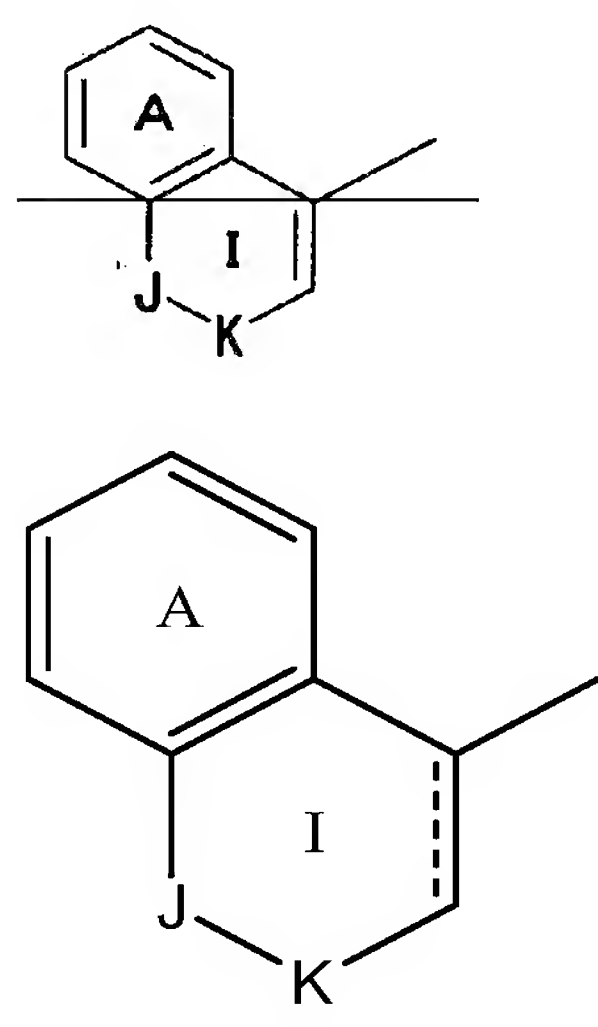
At page 22, lines 5-8, please replace the existing paragraph with the following new paragraph:

~~is a single bond or a double bond, ring R is a phenylene group optionally having substituent(s), and ring I optionally has substituent(s), or a salt thereof or a prodrug thereof,~~

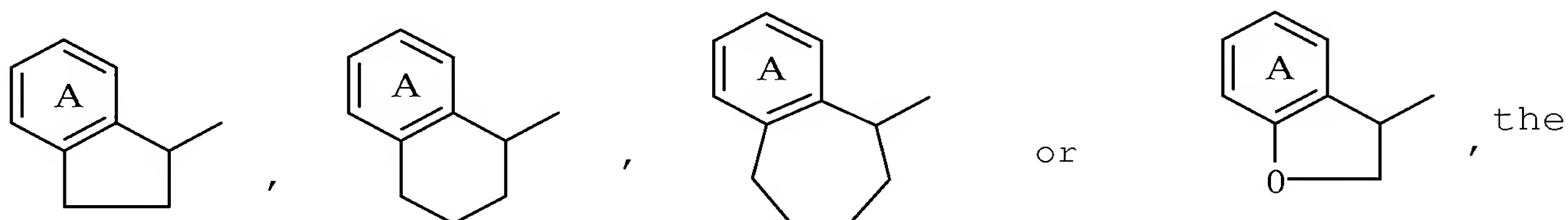
is a single bond or a double bond, ring R is a phenylene group optionally having substituent(s), and ring I optionally has substituent(s), or a salt thereof or a prodrug thereof,

At page 22, lines 9-19, please replace the existing paragraph with the following new paragraph:

[84] the ~~compound~~ regulator of the above-mentioned [83], wherein the partial structural formula



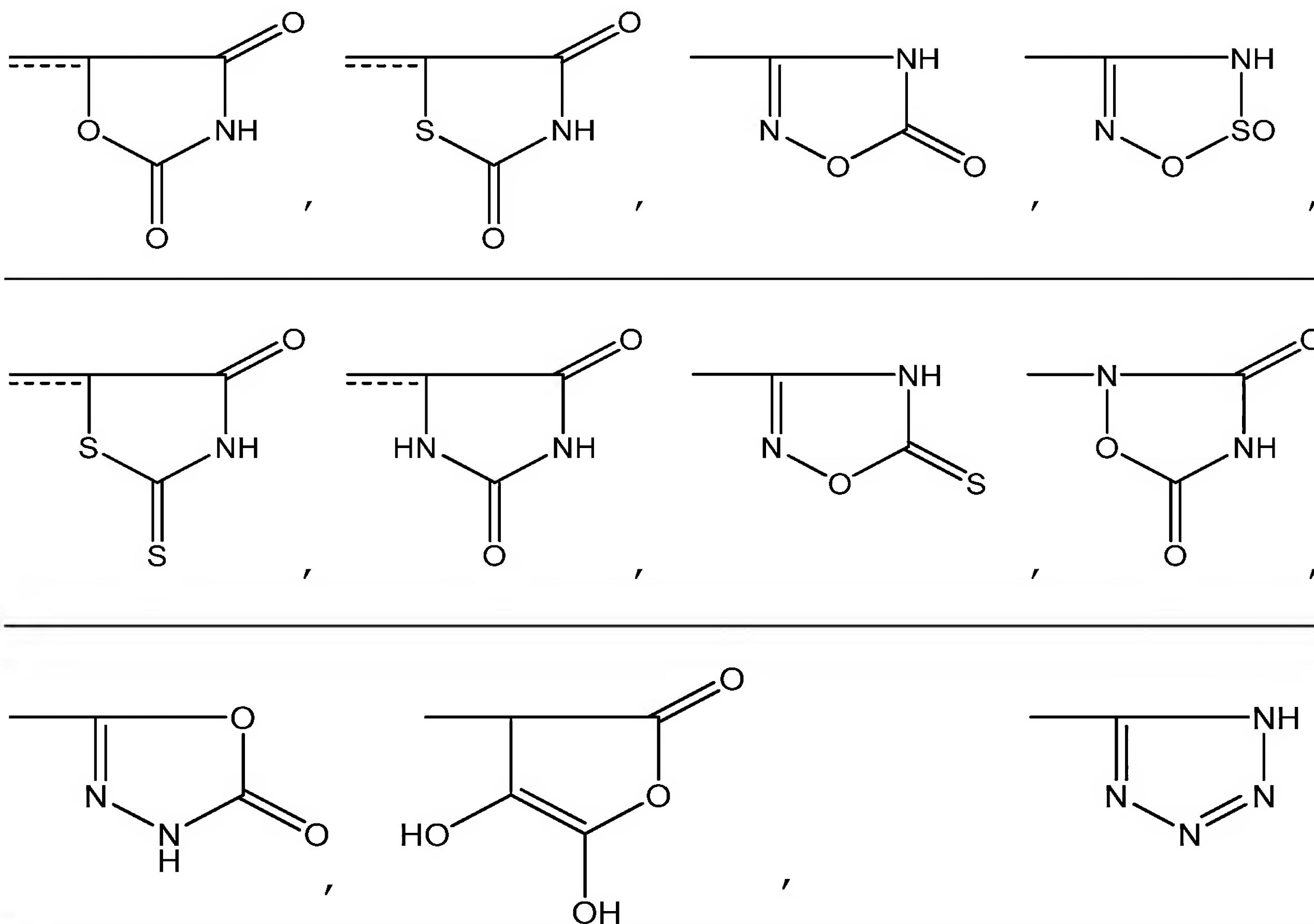
is

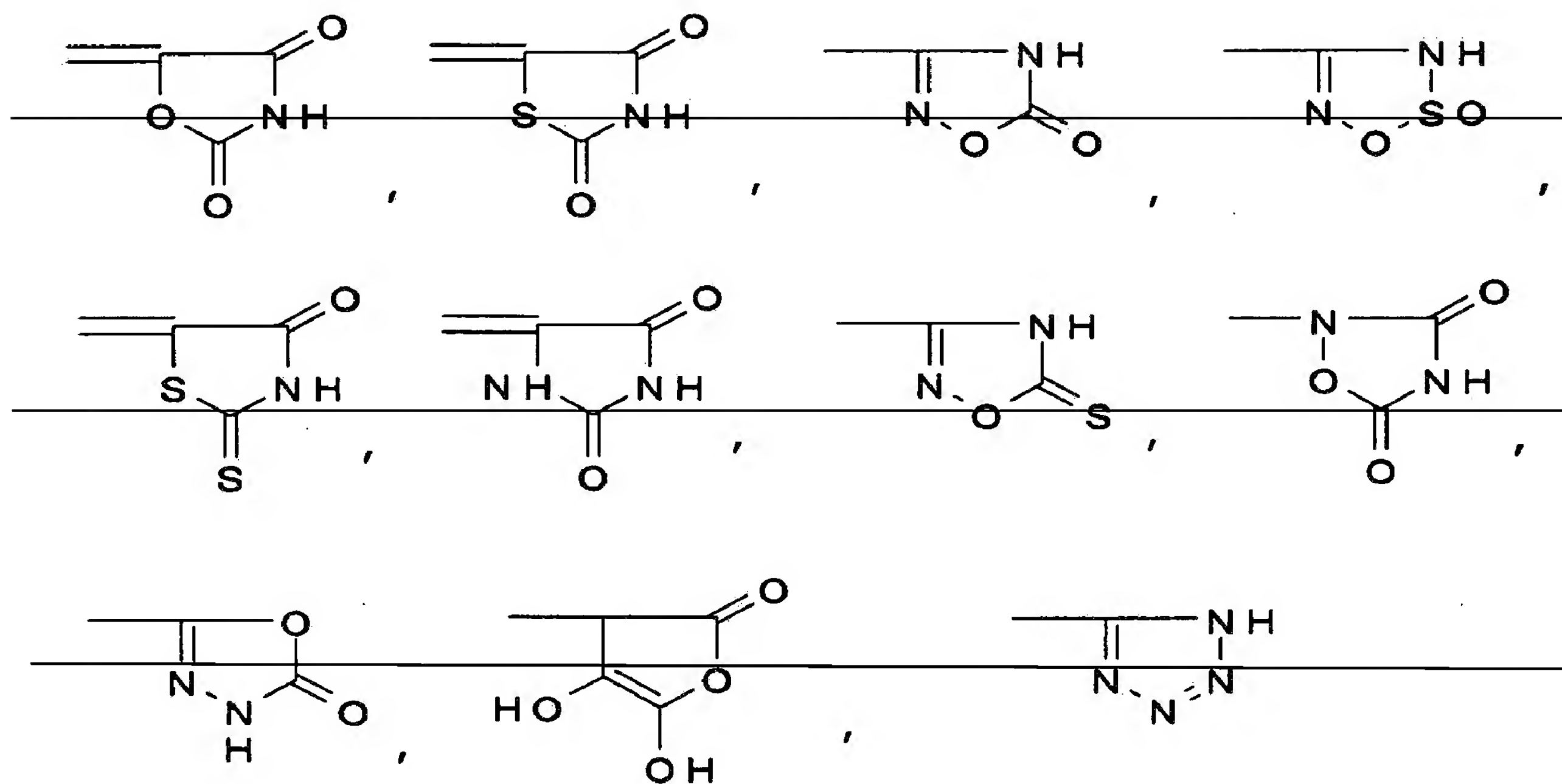


substituent of ring A is (i) a halogen atom, (ii) a C₁₋₆ alkyl group, (iii) a C₁₋₆ alkoxy group, (iv) a C₆₋₁₄ aryl group optionally having substituent(s) selected from a halogen atom and a C₁₋₆ alkyl, (v) a C₆₋₁₄ aryloxy group or (vi) a C₇₋₁₅ aralkyloxy group, and the substituent of ring R is a halogen atom, ~~or a salt thereof or a prodrug thereof,~~ and

At page 25, line 19 - end of page 25, please replace the existing paragraph with the following new paragraph:

As the above-mentioned 5-membered heterocyclic group capable of releasing cation, a 5-membered heterocyclic group comprising 1 to 4 selected from N, O and S as ring-constituting atom(s) and the like can be used. For example,

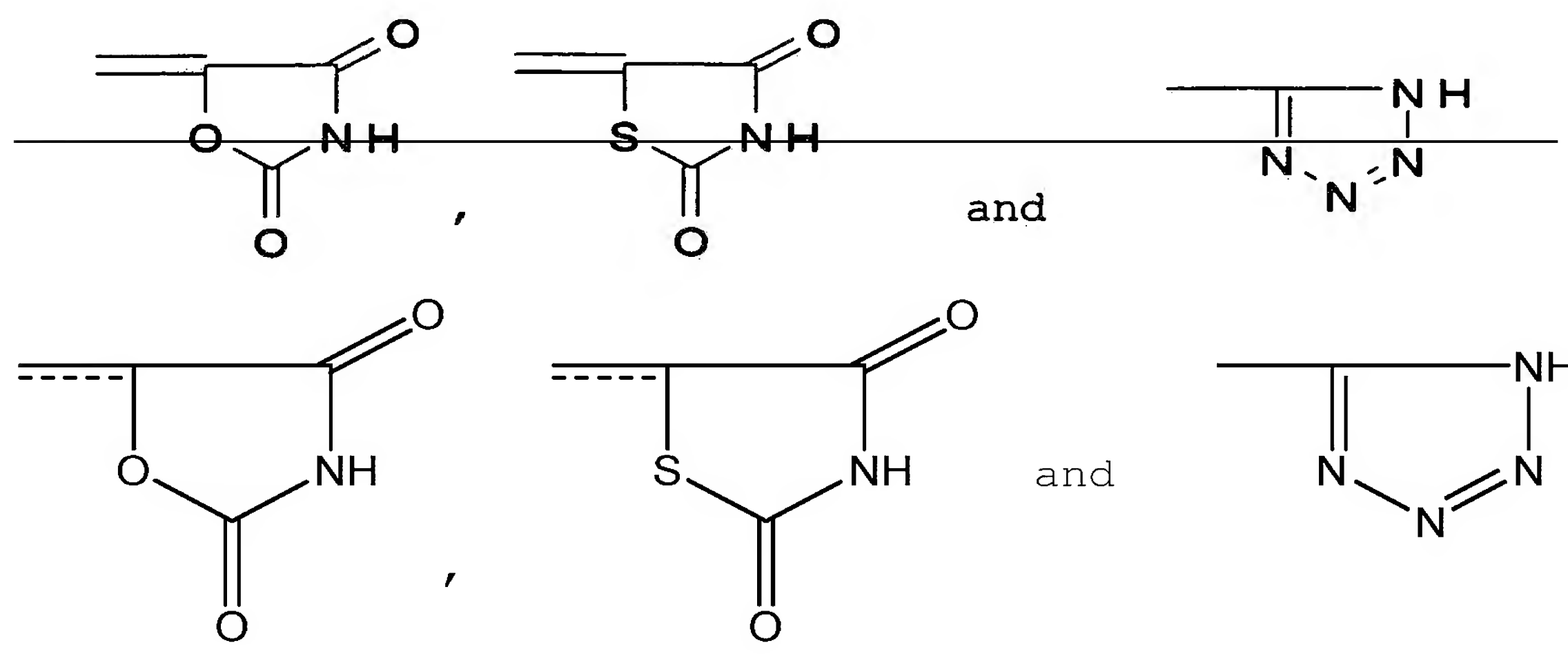




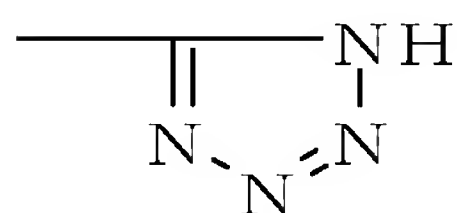
and the like can be mentioned.

At page 26, lines 2-6, please replace the existing paragraph with the following new paragraph:

Of these,



are preferable, and



is particularly preferable.

At page 30, line 16 – page 31, line 20, please replace the existing paragraph with the following new paragraph:

These "lower alkyl group", "lower alkenyl", "lower alkynyl", "lower alkoxy", "lower alkylthio", "lower alkyl-carbonyl", "lower alkyl-carbonylamino", "lower alkoxy-carbonylamino", "lower alkylsulfonylamino", "lower alkyl-carbonyloxy", "lower alkoxy-carbonyloxy", "mono-lower alkyl-carbamoyloxy" and "di-lower alkyl-carbamoyloxy" each optionally have, at substitutable position(s), 1 to 5 substituents selected from, for example, a halogen atom (e.g., fluorine atom, chlorine atom, bromine atom, iodine atom); hydroxy; amino; a ~~mono- or di-~~ 5- to 7-membered heterocyclic group containing, besides carbon atom, 1 or 2 kinds of 1 to 4 hetero atoms selected from a nitrogen atom, a sulfur atom and an oxygen atom (e.g., furyl, pyridyl, thienyl etc.) (said heterocyclic group being optionally substituted by a halogen atom, hydroxy, amino, optionally halogenated lower(C₁₋₆) alkyl, mono- or di-lower(C₁₋₆) alkylamino, mono- or di-C₆₋₁₄ arylamino, C₃₋₈ cycloalkyl, lower(C₁₋₆) alkoxy, lower(C₁₋₆) alkoxy-carbonyl, lower(C₁₋₆) alkylthio, lower(C₁₋₆) alkylsulfinyl, lower(C₁₋₆) alkylsulfonyl, the above-mentioned optionally esterified carboxyl, carbamoyl, thiocarbamoyl, mono-lower(C₁₋₆) alkyl-carbamoyl, di-lower(C₁₋₆) alkyl-carbamoyl, mono- or di-C₆₋₁₄ aryl-carbamoyl and the like); mono- or di-lower(C₁₋₆) alkylamino; mono- or di-C₆₋₁₄ arylamino; C₃₋₈ cycloalkyl; optionally halogenated lower(C₁₋₆) alkoxy; lower(C₁₋₆) alkoxy-

carbonyl; lower(C₁₋₆) alkylthio; lower(C₁₋₆) alkylsulfinyl; lower(C₁₋₆) alkylsulfonyl; the above-mentioned optionally esterified carboxyl; carbamoyl; thiocarbamoyl; mono-lower(C₁₋₆) alkyl-carbamoyl (e.g., methylcarbamoyl, ethylcarbamoyl etc.); di-lower(C₁₋₆) alkyl-carbamoyl (e.g., dimethylcarbamoyl, diethylcarbamoyl, ethylmethylcarbamoyl etc.); mono- or di-C₆₋₁₄ aryl-carbamoyl (e.g., phenylcarbamoyl, 1-naphthylcarbamoyl, 2-naphthylcarbamoyl etc.); mono- or di- 5- to 7-membered heterocyclylcarbamoyl containing, (besides carbon atom), 1 or 2 kinds of 1 to 4 hetero atoms selected from a nitrogen atom, a sulfur atom and an oxygen atom (e.g., 2-pyridylcarbamoyl, 3-pyridylcarbamoyl, 4-pyridylcarbamoyl, 2-thienylcarbamoyl, 3-thienylcarbamoyl etc.); C₁₋₆ alkyl-carbonylamino (e.g., acetylamino, propionylamino) optionally substituted by carboxy; and the like.


At page 33, line 26 – page 35, line 27, please replace the existing paragraph with the following new paragraph:


These "C₃₋₈ cycloalkyl", "C₃₋₈ cycloalkyl-carbonyl", "C₃₋₈ cycloalkyl-carbonylamino", "5 to 7-membered heterocyclylcarbonyl containing, besides carbon atom, 1 or 2 kinds of 1 to 4 hetero atoms selected from a nitrogen atom, a sulfur atom and an oxygen atom", "C₆₋₁₄ aryloxy", "C₇₋₁₆ aralkyloxy", "C₆₋₁₄ arylthio", "C₇₋₁₆ aralkylthio", "C₆₋₁₄ aryl-carbonyl", "C₇₋₁₆ aralkyl-carbonyl", "C₆₋₁₄ aryl-carbonylamino", "C₆₋₁₄ aryl-carbonyloxy", "mono- or di-C₆₋₁₄ aryl-carbamoyloxy", "C₆₋₁₄ arylsulfonyl", "C₆₋₁₄ arylsulfinyl", "C₆₋₁₄ arylsulfonylamino" and "aromatic heterocyclyloxy" each optionally have, at substitutable position(s), 1 to 5 substituents selected from, for example, a halogen atom (e.g., fluorine atom, chlorine atom, bromine atom, iodine atom); hydroxy; amino; the above-mentioned optionally substituted lower alkyl; the above-mentioned optionally substituted lower alkenyl; the above-mentioned optionally substituted lower alkynyl; C₆₋₁₄ aryl (said C₆₋₁₄ aryl is optionally substituted by a halogen atom, hydroxy, amino, optionally halogenated lower(C₁₋₆) alkyl, mono- or di-lower(C₁₋₆) alkylamino, mono- or di-C₆₋₁₄ arylamino, C₃₋₈ cycloalkyl, lower(C₁₋₆) alkoxy, lower(C₁₋₆) alkoxy-carbonyl, lower(C₁₋₆) alkylthio, lower(C₁₋₆) alkylsulfinyl, lower(C₁₋₆) alkylsulfonyl, the above-mentioned optionally esterified carboxyl, carbamoyl, thiocarbamoyl, mono-lower(C₁₋₆) alkyl-carbamoyl, di-lower(C₁₋₆) alkyl-carbamoyl, mono- or di-C₆₋₁₄ aryl-carbamoyl and the like); C₆₋₁₄ aryloxy (said C₆₋₁₄ aryloxy is optionally substituted by a halogen atom, hydroxy, amino, optionally halogenated lower(C₁₋₆) alkyl, mono- or di-lower(C₁₋₆) alkylamino, mono- or di-C₆₋₁₄ arylamino, C₃₋₈ cycloalkyl, lower(C₁₋₆) alkoxy, lower(C₁₋₆) alkoxy-carbonyl, lower(C₁₋₆) alkylthio, lower(C₁₋₆) alkylsulfinyl, lower(C₁₋₆) alkylsulfonyl, the above-

mentioned optionally esterified carboxyl, carbamoyl, thiocarbamoyl, mono-lower(C₁₋₆) alkyl-carbamoyl, di-lower(C₁₋₆) alkyl-carbamoyl, mono- or di-C₆₋₁₄ aryl-carbamoyl and the like); C₇₋₁₆ aralkyloxy (said C₇₋₁₆ aralkyloxy is optionally substituted by a halogen atom, hydroxy, amino, optionally halogenated lower(C₁₋₆) alkyl, mono- or di-lower(C₁₋₆) alkylamino, mono- or di-C₆₋₁₄ arylamino, C₃₋₈ cycloalkyl, lower(C₁₋₆) alkoxy, lower(C₁₋₆) alkoxy-carbonyl, lower(C₁₋₆) alkylthio, lower(C₁₋₆) alkylsulfinyl, lower(C₁₋₆) alkylsulfonyl, the above-mentioned optionally esterified carboxyl, carbamoyl, thiocarbamoyl, mono-lower(C₁₋₆) alkyl-carbamoyl, di-lower(C₁₋₆) alkyl-carbamoyl, mono- or di-C₆₋₁₄ aryl-carbamoyl and the like); a ~~mono- or di-~~5- to 7-membered heterocyclic group containing, besides carbon atom, 1 or 2 kinds of 1 to 4 hetero atoms selected from a nitrogen atom, a sulfur atom and an oxygen atom (e.g., furyl, pyridyl, thienyl etc.) (said heterocyclic group is optionally substituted by a halogen atom, hydroxy, amino, mono- or di-lower(C₁₋₆) alkylamino, mono- or di-C₆₋₁₄ arylamino, C₃₋₈ cycloalkyl, lower(C₁₋₆) alkoxy, lower(C₁₋₆) alkoxy-carbonyl, lower(C₁₋₆) alkylthio, lower(C₁₋₆) alkylsulfinyl, lower(C₁₋₆) alkylsulfonyl, the above-mentioned optionally esterified carboxyl, carbamoyl, thiocarbamoyl, mono-lower(C₁₋₆) alkyl-carbamoyl, di-lower(C₁₋₆) alkyl-carbamoyl, mono- or di-C₆₋₁₄ aryl-carbamoyl and the like); mono- or di-lower(C₁₋₆) alkylamino; mono- or di-C₆₋₁₄ arylamino; C₃₋₈ cycloalkyl; the above-mentioned optionally substituted lower(C₁₋₆) alkoxy; lower(C₁₋₆) alkoxy-carbonyl; lower(C₁₋₆) alkylthio; lower(C₁₋₆) alkylsulfinyl; lower(C₁₋₆) alkylsulfonyl; the above-mentioned optionally esterified carboxyl; carbamoyl; thiocarbamoyl; mono-lower(C₁₋₆) alkyl-carbamoyl (e.g., methylcarbamoyl, ethylcarbamoyl etc.); di-lower(C₁₋₆) alkyl-carbamoyl (e.g., dimethylcarbamoyl, diethylcarbamoyl, ethylmethylcarbamoyl etc.); mono- or di-C₆₋₁₄ aryl-carbamoyl (e.g., phenylcarbamoyl, 1-

naphthylcarbamoyl, 2-naphthylcarbamoyl etc.); mono- or di- 5- to 7-membered heterocyclylcarbamoyl containing, besides carbon atom, 1 or 2 kinds of 1 to 4 hetero atoms selected from a nitrogen atom, a sulfur atom and an oxygen atom (e.g., 2-pyridylcarbamoyl, 3-pyridylcarbamoyl, 4-pyridylcarbamoyl, 2-thienylcarbamoyl, 3-thienylcarbamoyl etc.) and the like.

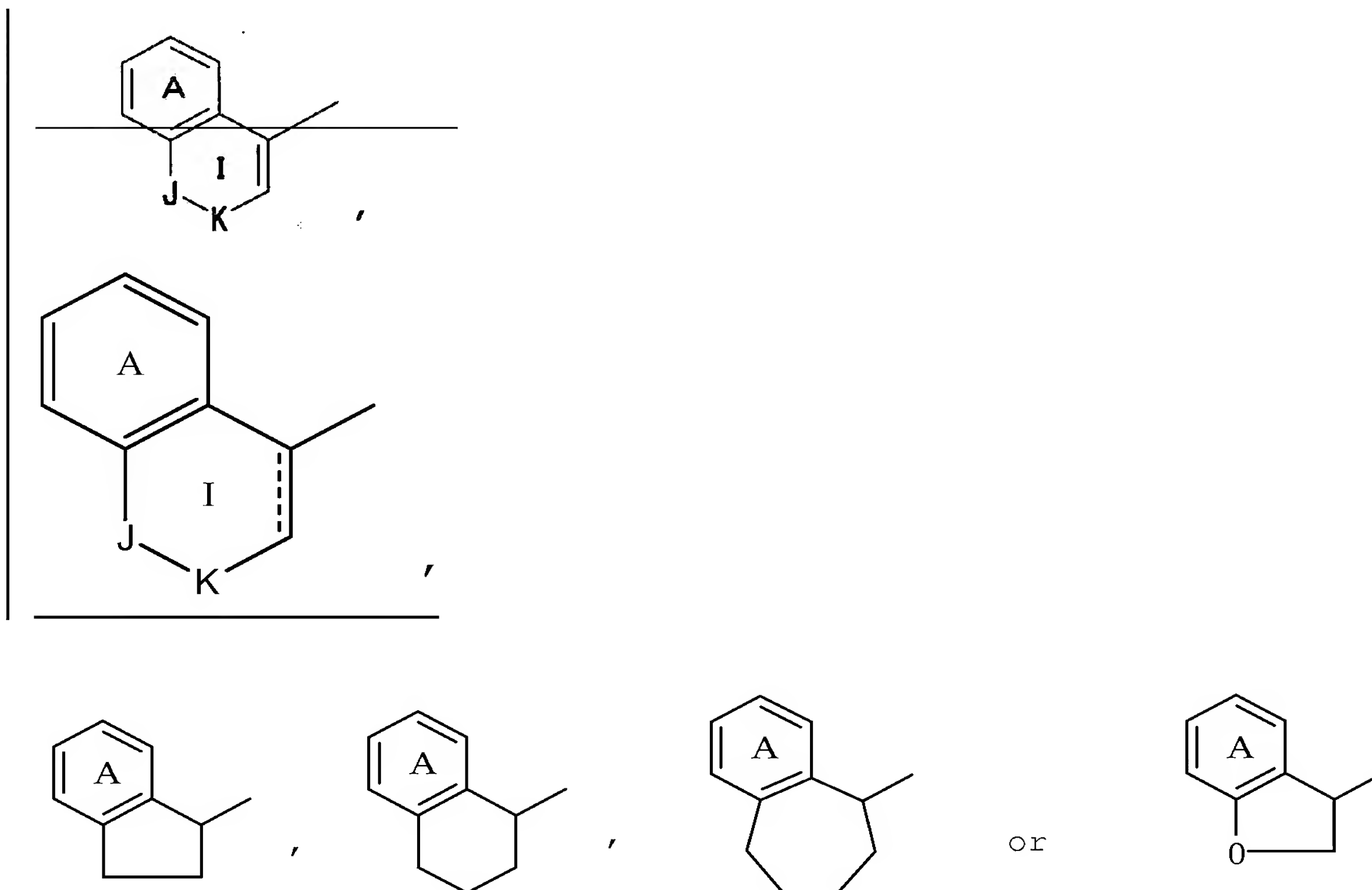
At page 55, lines 27-29, please replace the existing paragraph with the following new paragraph:

~~As K, a bond and methylene are preferable.~~
~~~~
~~is a single bond or a double bond.~~

As K, a bond and methylene are preferable.

is a single bond or a double bond.

At page 56, lines 3-17, please replace the existing paragraph with the following new paragraph:

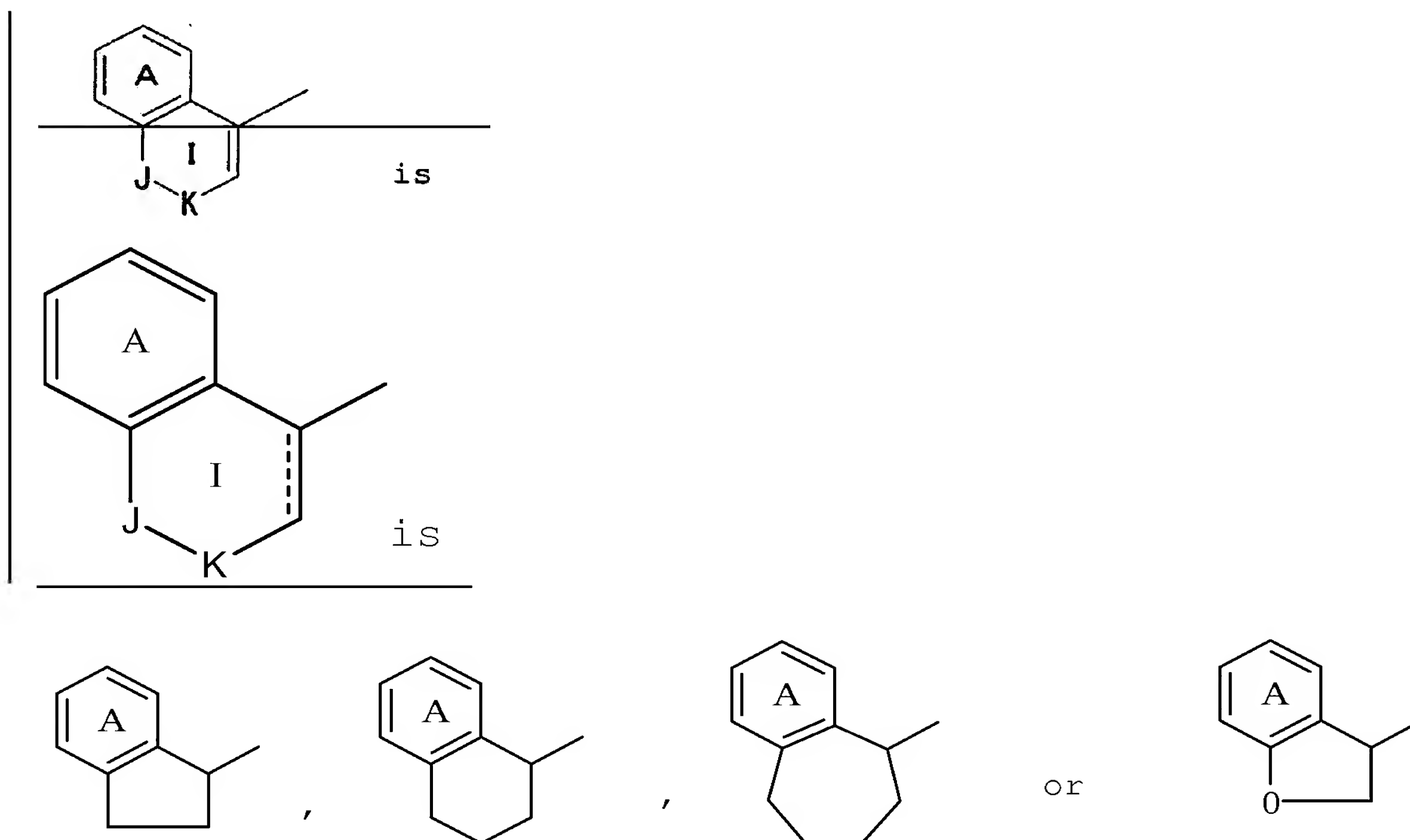
As the partial structural formula



and the like are preferable. As the substituent for ring A in this case, (i) a halogen atom, (ii) a C₁₋₆ alkyl group (e.g., methyl, ethyl, propyl), (iii) a C₁₋₆ alkoxy group (e.g., methoxy, ethoxy), (iv) a C₆₋₁₄ aryl group (e.g., phenyl, naphthyl) optionally having substituent(s) selected from a halogen atom (e.g., fluorine atom, chlorine atom, bromine atom) and a C₁₋₆ alkyl (e.g., methyl, ethyl, propyl), (v) a C₆₋₁₄ aryloxy group (e.g., phenyloxy) and (vi) a C₇₋₁₅ aralkyloxy group (e.g., naphthyloxy), are preferable, and as the substituent of ring R, a halogen atom (e.g., fluorine atom, chlorine atom, bromine atom) is preferable.

At page 58, line 16 – page 59, line 2, please replace the existing paragraph with the following new paragraph:

A compound (D) wherein the partial structural formula



wherein the substituent of ring A is (i) a halogen atom, (ii) a C₁₋₆ alkyl group, (iii) a C₁₋₆ alkoxy group, (iv) a C₆₋₁₄ aryl group optionally having substituent(s) selected from a halogen atom and a C₁₋₆ alkyl, (v) a C₆₋₁₄ aryloxy group or (vi) a C₇₋₁₅ aralkyloxy group, and the substituent of ring R is a halogen atom, is preferable.

At page 91, line 30 – page 92, line 5, please replace the existing paragraph with the following new paragraph:

As the carboxy-protecting group, for example, C₁₋₆ alkyl (e.g., methyl, ethyl, propyl, isopropyl, butyl, tert-butyl and

the like), phenyl, trityl or silyl and the like, each of which optionally has substituent(s), can be mentioned. As the substituent, a halogen atom (e.g., fluorine, chlorine, bromine, iodine and the like), formyl, C₁₋₆ alkyl-carbonyl (e.g., acetyl, propionyl, butylcarbonyl and the like), nitro, C₁₋₆ alkyl (e.g., methyl, ethyl, tert-butyl and the like), ~~C₄₋₆ aryl~~ C₆₋₁₀ aryl (e.g., phenyl, naphthyl and the like) and the like can be used. The number of the substituent is about 1 to 3.

At page 209, lines 32-35, please replace the existing paragraph with the following new paragraph:

The title compound was obtained from methyl 4-[(5-bromo-2-chlorophenyl)methoxy]benzenepropanoate by a method similar to that of Reference Example 4. yield 66%, ~~yield 81%~~.

At page 210, lines 17-19, please replace the existing paragraph with the following new paragraph:

The title compound was obtained from methyl 4-[(3-bromo-4-chlorophenyl)methoxy]benzenepropanoate by a method similar to that of Reference Example 4. ~~yield 81%, yield 81%~~.

At page 212, lines 23-24, please replace the existing paragraph with the following new paragraph:

melting point: 146-147°C (recrystallized from ethyl acetate-hexane) .

At page 253, lines 18-22, please replace the existing paragraph with the following new paragraph:

The title compound was obtained from methyl 4-hydroxybenzenepropanoate and 2-benzothiazolemethanol by a method similar to that of Example 105. yield 91%.

~~melting point: °C (recrystallized from ethyl acetate-diisopropyl ether).~~

At page 279, lines 16-18, please replace the existing paragraph with the following new paragraph:

Example 199 methyl 4-[[3'-[[(3-carboxy-1-oxopropyl) amino]methyl]-[1,1'-biphenyl]-3-yl]methoxy]benzenepropanoic acid~~benzenepropanoate~~